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Prognostic factors and outcomes in patients with acute COPD exacerbation in intensive care unit: Systematic review

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ABSTRACT

Background: Chronic obstructive pulmonary disease is one of the common causes of death worldwide and is a common lung illness that causes respiratory failure in adults. This study aimed to investigate prognostic variables and mortality in COPD patients admitted to the intensive care unit. **Method:** The PRISMA standards were followed in the conduct of this investigation, and the systematic review included electronic searches of MEDLINE, Embase, Cochrane Library, CINAHL, and Web of Science. We combined COPD-related search terms with prognostic factors, triggers, clinical outcomes, and research design. We looked through electronic databases for English-language publications from 2013 to 2023 that described acute COPD exacerbation in patients admitted to the intensive care unit. **Result:** In our study, the mean age range of patients is 67.3 to 84. The range of hospital mortality is 11.5% to 29%. The following prognostic factors were examined: age, initial CRP greater than 7.5 mg/dL, elevated BUN, decreased MAP, intubation incident, and use of vasopressors, persistent cardiac failure, less than $0.8 \times 10^9/L$ for lymphocytes, less than $4 \times 10^9/L$ for white blood cells, male gender, and less than 88% SpO₂ in the first 24 hours. **Conclusion:** Variables associated with hospital mortality were advanced age, high initial CRP, low peak ENR on days 8–14 of treatment, lymphocytes fewer than $0.8 \times 10^9/L$, leukopenia, need for invasive mechanical ventilation, CHF, and in-hospital comorbidities among patients with acute COPD exacerbations requiring ICU admission.

Keywords: Chronic obstructive pulmonary disease, prognostic variables, mortality, intensive care unit

1. INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is the fourth greatest cause of death worldwide and is a common lung illness that causes respiratory failure in adults (Cote and Celli et al., 2007). Most often, cigarette smoking is associated with COPD, although pollution from the environment also has an impact. COPD is also significantly influenced by smoke from domestic stoves and occupational air pollution (Vogelmeier et al., 2017). Some individuals experience a progressive loss of respiratory function as a result of the condition. When someone has a history of being exposed to the disease's risk factors, produces sputum from a persistent cough, and exhibits dyspnea, they should be diagnosed with COPD. Acute exacerbations break the clinical course of COPD and cause acute respiratory symptoms to worsen.

In severe cases, this calls for hospitalization and the use of supplemental medication. In the intensive care unit (ICU), where non-invasive and non-invasive mechanical ventilation (MV) is used to treat acute respiratory failure, acute COPD exacerbations are frequently the reason for admission (Vogelmeier et al., 2017). Acute COPD exacerbations account for 2% of all ICU admissions (Berenyi et al., 2020). Prior research has indicated that exacerbation is not always the main cause of the sudden deterioration in COPD patients; pulmonary edema, pneumonia, cardiac arrhythmias, pneumothorax, surgery, pulmonary embolism, and sepsis may also be to blame (Afessa et al., 2002; Ucgun et al., 2006).

Exacerbations of COPD are a major cause of mortality and morbidity. A COPD exacerbation has been linked to reported in-hospital mortality ranging from 11% to 32% (Afessa et al., 2002; Gadre et al., 2018). Examining mortality and prognostic factors in COPD patients hospitalized to the ICU was the goal of this study. In addition, we planned to investigate the factors linked to short-term mortality in this study.

2. METHOD

This study was conducted according to PRISMA guidelines, electronic searches of MEDLINE, Embase, Cochrane Library, CINAHL, and Web of Science are part of the systematic review. We incorporated prognostic variables, triggers, clinical outcomes, and research design with COPD-related search phrases. We searched the electronic databases for articles published in the English language in the period from 2013 to 2023 reporting acute COPD exacerbation in ICU-admitted patients. Among the prognostic factors for COPD that could indicate systemic issues were: APACHE II score; vasopressor use; Elevated blood urea nitrogen (BUN); lower mean arterial pressure (MAP); intubation event; C-reactive protein CRP; age; comorbidities; gender; SpO₂; White blood cell count; Lymphocyte count.

The selection and review of the articles were carried out separately by two reviewers. Cross-referencing was done on full-text papers and reviews that turned up during the first search. The following studies met the requirements for full-text paper selection: (1) original research; (2) COPD exacerbation sample size of 100 or more; (3) evaluation of a pertinent prognostic factor; (4) full-text paper in English; (5) general population; and (6) record mortality rate. Citation, sample sizes, death rate, mean patient age, prognostic factors, and key findings were taken from included studies in a pre-designed Google sheet and Google document. Odds ratios for prognostic factors were collected, both adjusted and unadjusted, if possible.

3. RESULT

We included 5 studies (Figure 1) in our review with a total of 1136 patients. Mean patient's age ranged from 67.3 Limsuwat et al. (2013) to 84 (Chen et al., 2019). In-hospital mortality ranges from 11.5% Cao et al., (2021) to 29% (Akbaş et al., 2023). Prognostic factor studied include; APACHE II score, and vasopressor use Akbaş et al., (2023), Elevated BUN, lower MAP, and intubation event Limsuwat et al., (2013), First CRP more than 7.5 mg/dL, and age Chen et al., (2019), Chronic heart failure, Lymphocyte count less than $0.8 \times 10^9/L$, White blood cell count less than $4 \times 10^9/L$ Cao et al., (2021), Male gender and SpO₂ less than 88% in the first 24 h (Sandau et al., 2022) (Table 1).

The following were the most commonly reported negative prognostic mortality factors in acute COPD exacerbation ICU cases: Low MAP; elevated BUN Limsuwat et al., (2013); an intubation event Limsuwat et al., (2013), Cao et al., (2021); a lower value of initial SpO₂ at admission Sandau et al., (2022); lymphocytes less than $0.8 \times 10^9/L$; chronic heart failure; leukopenia Cao et al., (2021); Sandau et al., (2022); older age, an initial C-reactive protein more than 7.5 mg/dL; a peak eosinophil to neutrophil ratio of less than 102; and in-hospital complications (Chen et al., 2019). Additionally, APACHE II score, albumin levels at admission, PaO₂/FIO₂ ratio at admission,

and the vasopressor use medications throughout an ICU stay were shown to be predictive of death in a recently published study (Akbaş et al., 2023).

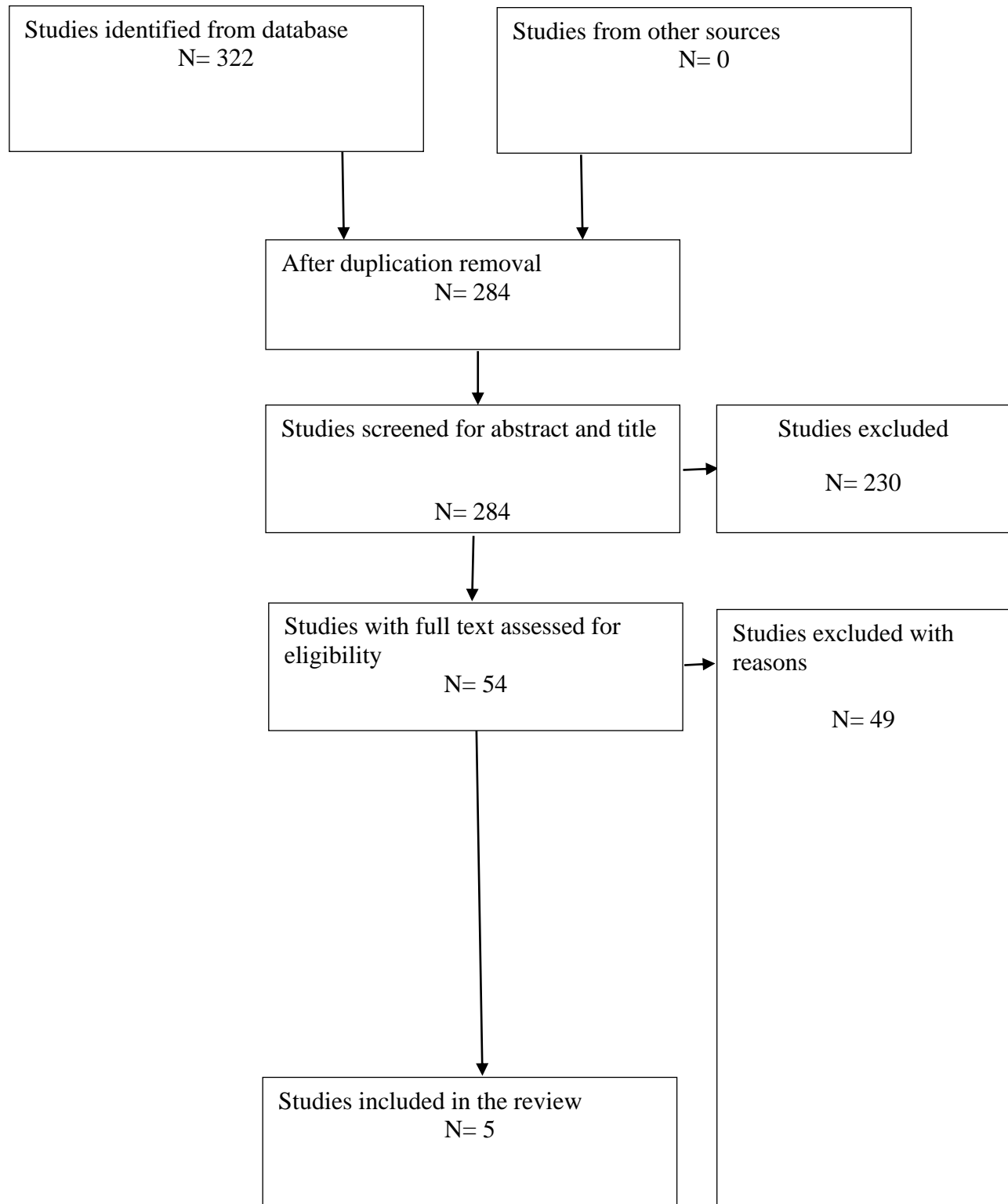


Figure 1 PRISMA consort chart

In particular, we discovered information regarding the triggers of COPD exacerbations with hypercapnic acute respiratory failure needing ICU admission in Akbaş et al., (2023) study, which names pneumonia, heart failure and acute bronchitis, as the main causes of COPD exacerbations. Finding the predictors of mortality in COPD patients needing ICU admission was the only study goal; no information regarding the infectious aetiological agents was provided. Furthermore, this study's primary drawback was its retrospective nature (Table 2).

Table 1 Characteristic of the included studies

Citation	Type of the study	Number of patients	Mortality rate	Mean age of patients in years	Prognostic factor	Odd ratio
Akbaş et al., 2023	Observational retrospective	100	29%	71.6	APACHE II score, vasopressor use	APACHE II score 1.2, vasopressor use= 8.3
Limsuwat et al., 2013	Observational, retrospective study	217	12%	67.3	Elevated BUN, lower MAP, intubation event	elevated BUN= 1.06, lower MAP= 0.91, intubation event= 6.1
Chen et al., 2019	Retrospective case-control study	146	16.4%	84	First CRP > 7.5 mg/dL, and age	First CRP > 7.5 mg/dL= 4.5, age = 1.12
Cao et al., 2021	Observational, retrospective	384	11.5%	78.2	Chronic heart failure, Lymphocyte count <0.8 × 10 ⁹ /L, White blood cell count <4 × 10 ⁹ /L	chronic heart failure= 30.3, Lymphocyte count <0.8 × 10 ⁹ /L= 3.6, White blood cell count <4 × 10 ⁹ /L= 5.7
Sandau et al., 2022	Observational, retrospective study	289	18%	74.8	Male gender, SpO ₂ < 88% in the first 24 h	Male gender= 1.8, SpO ₂ < 88% in the first 24 h= 2.4

Table 2 Main findings of the included studies

Citation	Main findings	Conclusion
Akbaş et al., 2023	A hundred patients underwent evaluation. Acute hypercapnic respiratory failure was primarily caused by pneumonia, bronchitis and heart failure. The patients had an invasive MV rate of 43% and a mean Acute Physiology and Chronic Health Evaluation (APACHE) II score of 23. The death rates in the ICU, hospital, and 90 days were 21%, 29%, and 39%, correspondingly. In addition to higher APACHE II scores, longer ICU and hospital stays, poorer entry albumin levels and PaO ₂ /FiO ₂ ratios, and more pneumonia, invasive MV, shock within the first 24 hours of admission, renal replacement treatment, and vasopressor use, non-survivors also shared these characteristics. Admission PaO ₂ /FiO ₂ ratio, the usage of vasopressors, and APACHE II score were found to be predictive of ICU mortality by logistic regression analysis. APACHE II score and	Vasopressor use, albumin levels, APACHE II scores, and the PaO ₂ /FiO ₂ ratio are important indicators of short-term mortality in critically ill COPD patients experiencing acute hypercapnic respiratory failure.

	the admission albumin level were found to be predictive of 90-day mortality.	
Limsuwat et al., 2013	The survivors' mean age was 66.4 years, while the in-hospital death group's mean age was 70.4 years. The death rate as a whole was 12%. The results of multivariate analysis demonstrated a strong correlation between the death rate, intubation events, and low mean arterial blood pressure (MAP), and increased BUN.	This study determined the clinical characteristics linked to higher fatality rates among patients with acute COPD exacerbation hospitalized to an ICU. These indicators, which are easily collected during the patient's initial evaluation, include a low MAP, intubation, and a high BUN. The intensity of the acute aggravation and problems in other organ systems are reflected in them.
Chen et al., 2019	Age, peak eosinophil-toneutrophil ratio, in-hospital problems, and C-reactive protein (CRP) level >7.5 mg/dL at the emergency room were found to be variables associated with hospital mortality by multivariate logistic regression analysis. Following receiver operating characteristic curve investigations, a cutoff value of 0.224 was determined for peak ENRH102.	In patients with acute COPD exacerbation needing ICU admission, initial CRP >7.5 mg/dL, older age, in-hospital comorbidities, and peak ENR on days 8–14, were linked to hospital death. Hospital mortality was higher in patients with both indicators, starting CRP >7.5 mg/dL, and peak ENR <0.224 on days 8–14 of therapy.
Cao et al., 2021	Of the hospitalized patients, 11.5% died while 88.5% were released. Respiratory failure accounted for 76.6% of all comorbidities, with hypertension coming in second at 55.7%, coronary heart disease at 29.9%, and chronic heart failure at 19.8%. The need for invasive MV, leukopenia, lymphocytopenia, and chronic heart failure were independent risk factors linked to in-hospital mortality.	Patients who require ICU admission due to an acute exacerbation of COPD have a significant in-hospital death rate. Leukopenia, requiring invasive MV, lymphocytes < 0.8 × 10 ⁹ /L, and chronic heart failure were found to be risk factors linked to higher death rates.
Sandau et al., 2022	A low number of days alive and 14 days discharged were linked to at least one hypoxemia incident during the first 24 hours. Within the first 24 hours of admission, a minimum of one measurement of hyperoxemia did not correlate with a low number of days alive and discharged from the hospital within 14 days.	Being hypoxemic at any point in the first 24 hours following admission is linked to a much higher risk of a poor prognosis for patients with acute COPD exacerbation.

4. DISCUSSION

According to Akbaş et al., (2023) study, patients with high illness severity scores were admitted to the ICU if they developed acute hypercapnic respiratory failure, regardless of the cause. A quarter of patients passed away in the ICU, and almost half of them needed invasive MV. Renal replacement treatment, invasive MV, pneumonia, and the use of vasopressors were all more common in non-survivors than in survivors. Non-survivors also had low albumin levels, prolonged ICU and hospital stays, high APACHE II scores, and low PaO₂/FiO₂ ratios. Vasopressor use, APACHE II scores, and the PaO₂/FiO₂ ratios were found to be predictive of ICU mortality; APACHE II scores and serum albumin levels were found to be predictive of 90-day mortality (Akbaş et al., 2023). Specifically, lower than 0.8×10⁹/L lymphocytes, leukopenia, need for invasive MV, and having CHF were linked to increased risk of in-hospital death (Cao et al., 2021).

Previous research has found several risk variables that predict death from acute COPD exacerbations. Several factors, including CRP, the ratio of neutrophils to lymphocytes, the ratio of platelets to lymphocytes, the value of D-dimers, and the N-terminal prohormone B-type natriuretic peptide, have been linked to in-hospital mortality in patients with acute COPD exacerbations (Dahl et al., 2007; Miniati et al., 2011; Yao et al., 2017). The underlying severity of the acute illness is reflected in variables linked to mortality following acute COPD exacerbations (Messer et al., 2012). Dyspnea, acidemia, and atrial fibrillation have been found by Steer et al., (2012) to be independent predictors of hospital mortality in patients admitted with acute COPD exacerbations.

Ongel et al., (2014) reported that comorbidities (hypertension, arrhythmia, and coronary artery disease) and clinical variables (invasive MV support, BMI <20 kg/m², pneumonia, chronic hypoxia, and high APACHE II scores) upon ICU admission were predictive of ICU mortality in patients with acute COPD exacerbations. Preadmission functional dependency, cognitive decline, corticosteroid use, and high NT-proBNP at admission were shown by Pannella et al. to be risk factors for mortality in the oldest patients (Spannella et al., 2019). In Chen et al., (2019) study, age, baseline CRP, and peak ENR levels on days 8 to 14 of treatment were independent predictors of death. Males, a lower body mass index, a lower PaO₂, severe hypercapnia, and the length of the ICU hospitalization are all strongly correlated with poorer survival and a greater probability of mortality during hospitalization (Hasegawa et al., 2014; Soler et al., 2005).

Furthermore, poor outcomes are linked to a lower body mass index, lower serum albumin levels, and a longer duration of the disease (Gunen et al., 2005). For individuals with severe COPD, anorexia, fatigue, and weight loss are daily limits. Patients may experience anxiety or depressive symptoms as a result of these limitations. When gathering information about a patient's medical history, it is important to ask specific questions about depression and anxiety because these conditions are not only common in people with COPD but also linked to a higher risk of new exacerbations and a worsening of health (Sin et al., 2006; Miller et al., 2013).

Furthermore, cardiovascular comorbidities—myocardial infarction, stroke, unstable angina, and transient ischemic attack, in particular—play a critical role in the history of COPD, the course of the disease, and acute COPD exacerbation outcomes in an ICU setting (Kunisaki et al., 2018; Hoiseth et al., 2011). Chronic renal failure, osteoarthritis, and diabetes mellitus are other significant factors that adversely affect the outcomes of COPD acute exacerbations (Singh et al., 2016). The factors that lead to the decline of acute COPD exacerbations in patients in an ICU include age, the requirement for invasive MV Brown et al., (2018), length of hospital stay, and problems during the ICU stay (Chen et al., 2019).

5. CONCLUSION

Among patients with acute COPD exacerbations needing ICU admission, variables linked to hospital mortality included advanced age, high starting CRP, low peak ENR on days 8–14 of treatment, lymphocytes fewer than $0.8 \times 10^9/L$, leukopenia, need for invasive MV, CHF, and in-hospital comorbidities. Patients with high illness severity scores were admitted to the ICU if they developed acute hypercapnic respiratory failure, regardless of the cause. Furthermore, invasive MV was needed for almost half of our patients, and one-fifth of them passed away in the ICU.

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This study has not received any external funding.

Ethical approval

Not applicable.

Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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